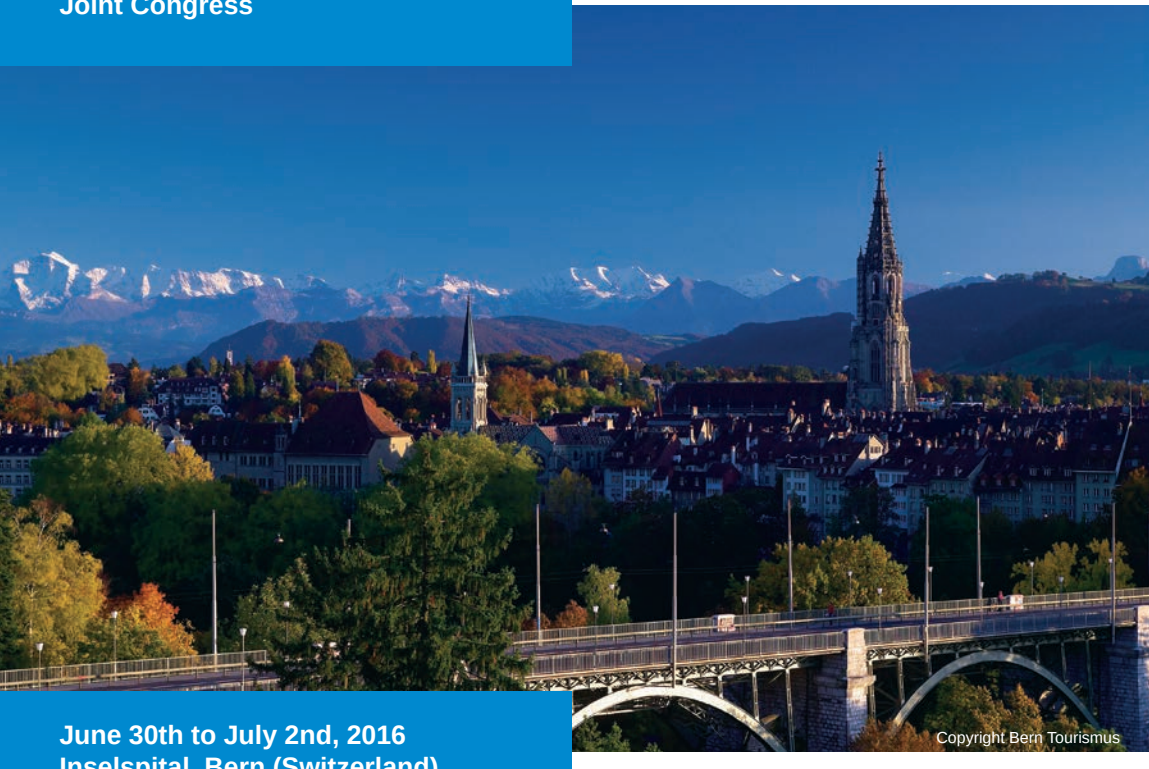
Schweizerische Gesellschaft für Endokrinologie und Diabetologie
Société Suisse d'Endocrinologie et de Diabétologie
Società Svizzera d'Endocrinologia e da Diabetologia
Societad Svizra d'Endocrinologia e Diabetologia

ZENTRALEUROPÄISCHE DIABETESGESELLSCHAFT

Joint Congress



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June 30th to July 2nd, 2016
Inselspital, Bern (Switzerland)

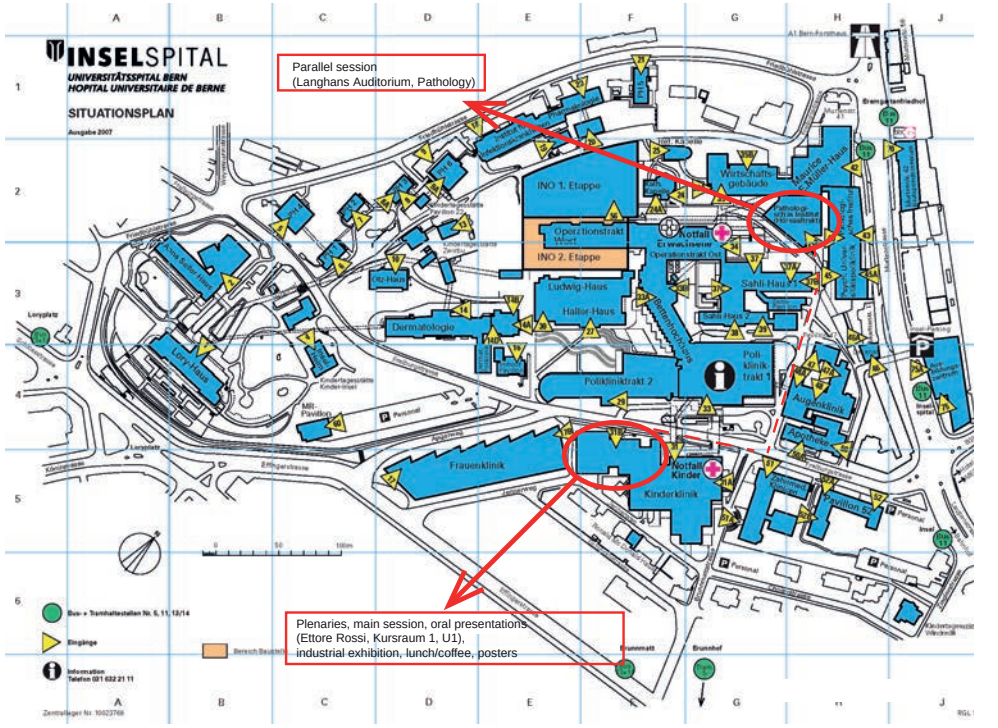
31st Congress of the Federation of International Danube Symposia on Diabetes mellitus

11th Congress of the Central European Diabetes Association

Spring-Meeting of the Swiss Society of Endocrinology and Diabetes

Contents

page



The SSED awards credits as follows:

<u>Thursday, June 30th</u>	
Symposium Boehringer Ingelheim	1 credit
Official program (1.45 pm to 5.40 pm)	4 credits
Symposium Novo Nordisk	1 credit
<u>Friday, July 01st</u>	
Official program (9 am to 5.20 pm	8 credits
Symposium Astra Zeneca	1 credit
<u>Saturday, July 02nd</u>	
Official program 8.15 am to 12.40 pm	4 credits
Total	19 credits

Liebe FID-Mitglieder

Liebe Mitglieder der Schweizerischen Gesellschaft für Endokrinologie und Diabetologie

Liebe Diabetes-Interessierte

Meinen Mitarbeitern und mir ist es eine grosse Freude, das 31. Donau-Symposium in Bern zu organisieren und Sie vom 30.6. bis 2.7.2016 zu diesem Symposium empfangen zu dürfen!

Erstmals finden der Kongress der Zentraleuropäischen Diabetesgesellschaft (CEDA) und das Donau-Symposium der FID gemeinsam mit der Frühjahrstagung der Schweizerischen Gesellschaft für Endokrinologie und Diabetologie in Bern statt. Wenn Sie sich fragen, was denn Bern mit der Donau zu tun habe und wieso gerade hier ein Donau-Symposium stattfinden soll, darf ich Sie auf http://aarelauf.ch/geologie-2/ (Stichwort „Aare-Donau") verweisen. Da werden Sie feststellen, dass vor Jahrmillionen die Aare, Wahrzeichen unserer Stadt, einer der Hauptzuflüsse der Donau war. Die Aare war nämlich im Laufe der geologischen Entwicklung nacheinander der Oberlauf der Donau, der Rhone und später des Rheins. Wahrlich eine Zentraleuropäische Region!

Wir haben für Sie ein Programm zusammengestellt, welches einerseits zahlreiche klinisch hochaktuelle Themen beleuchtet und Ihnen andererseits einen Einblick über die diabetologische Forschung in der Schweiz geben wird.

Auch touristisch und kulturell hat die Schweizer Hauptstadt einiges zu bieten. „Sie ist die Schönste, die wir je gesehen haben" schrieb jedenfalls Johann Wolfgang von Goethe in einem Brief an seine Freundin Charlotte von Stein, als er sich im Jahre 1779 in Bern aufhielt. Ein Besuch in Bern wird auch Ihnen Gelegenheit geben, sich von der homogenen Altstadt (UNESCO-Weltkulturerbe), der charakteristischen Aareschlaufe und dem überwältigenden Alpenpanorama verzaubern zu lassen.

Mit herzlichen Grüssen, und willkommen in Bern!

Prof. Dr. Peter Diem, Tagungspräsident

Thursday, June 30, 2016

11:15 – 12:00	**FID Board Meeting**	(Kursraum 4, U1)
12:30 – 13:30	**Lunch-Symposium:** **Beyond Glucose: From Surrogate Markers to Endpoints – The Impact of Outcome Studies in the Treatment of T2D** *(sponsored by Boehringer Ingelheim)*	(Auditorium Ettore Rossi)
	Chair: P. Diem, Bern H. Drexel, Feldkirch: Reduction of Mortality in High Risk Patients with Empagliflozin - Implications for Treatment Decisions in T2D A. Zanchi, Lausanne: Influence of Kidney Function on Treatment Choices in T2D - a Swiss Example	
13:45 – 14:10	**Welcome Address**	(Auditorium Ettore Rossi)
	R. Lehmann, Zurich; P. Diem , Bern	
14:10 – 15:30	**Opening Session**	(Auditorium Ettore Rossi)
	Chair: P. Diem, Bern; R. Lehmann, Zurich	
14:10 – 14:50	P. Scherrer, Dallas: The Role of the Adipose Tissue in Diabetes and Obesity	
14.50 – 15:30	H. Steinke, Bern: Johann Conrad Brunner and his Studies on Pancreatectomy	
15:30 – 16:00	**Coffee Break**	(Foyer, Kursraum 1)
16:00 – 17:40	**Session 1:** **Update on Novel Treatment Options in Diabetes and Metabolism**	(Auditorium Ettore Rossi)
	Chair: E. Christ, Bern; W. Waldhäusl, Vienna	
16:00 – 16:25	R. Weitgasser, Salzburg: New Insulins	
16:25 – 16:50	M. Nauck, Bochum: GLP1-Analogs	
16:50 – 17:15	C. Ehrenbichler, Innsbruck: New Treatment Options for Hypercholesterolemia	
17:15 – 17:40	N.C. Schloot, Dusseldorf: Diabetes Disease Classification: Relevance to Pathophysiology and Treatment	
17:40 – 18:00	**Coffee Break**	(Foyer, Kursraum 1)
18:00 – 19:00	**Satellite-Symposium:** **Beyond Glucose Lowering: GLP-1Effects on Body Weight and Cardiovascular System** *(Sponsored by Novo-Nordisk)*	(Auditorium Ettore Rossi)
	Chair: M. Donath, Basel Speakers: J.J. Holst, Copenhagen and S. Bilz, St. Gallen	
19:30	**Welcome Reception**	(Inselspital, Main Building, Top Floor)

Friday, July 01, 2016 (Program Auditorium Ettore Rossi)

08:15 – 09:00	**FID Plenary Meeting**	(Auditorium Ettore Rossi)
09:00 – 10:15	**Session 2:** **Hot Topics in Diabetes** *(supported by the Swiss Diabetes Foundation)*	(Auditorium Ettore Rossi)
	Chair: M. Brändle, St. Gallen; T. Temelkova-Kurtschiev, Sofia	
09:00 – 09:25	M. Roden, Dusseldorf: Adaptation of Energy Metabolism in NAFLD	
09:25 – 09:50	M. Brändle, St. Gallen: Health Economics of Diabetes for the Beginner	
09:50 – 10:15	V. Schwitzgebel, Geneva: Monogenetic Diabetes	
10:15 – 10:45	**Coffee Break**	(Foyer, Kursraum 1)
10:45 – 12:30	**Symposium:** **Technological Solutions to Address Challenges in Diabetes and Obesity** *(sponsored by Medtronic / Covidien)*	(Auditorium Ettore Rossi)
	Chair: M. Laimer, Bern; P. Kempler, Budapest R. Vigersky, Bethesda: What Role for Continuous Glucose Monitoring in T2 Diabetes? B. Guerci, Nancy: When Intensive Insulin Therapy Fails in Type 2 Diabetes: The Role of Pump Therapy T. Köstler, Schlieren/Basel: Update Bariatric Surgery: Which Conservative and Surgical Methods Are Available?" D. Kröll, Bern: Metabolic Surgery – An Update from Surgical Perspective Panel Discussion	
12:15 – 14:00	**Lunch**	(Foyer, Kursraum 1)
12:30 – 14:00	**Poster Session**	(Auditorium Ettore Rossi)
	Chair: T. Stulnig, Vienna; N. Lalic; Belgrade	
14:00 – 15:40	**Session 3:** **The Role of Alpha-Cells in Diabetes**	(Auditorium Ettore Rossi)
	Chair: J. Philippe, Geneva; M. Roden, Dusseldorf	
14:00 – 14:25	B. Thorens, Lausanne: Recognition and Reaction to Hypoglycemia	
14:25 – 14:50	F. Knop, Copenhagen: Regulation of Glucagen Secretion from the Alpha-Cells	
14:50 – 15:15	Y. Gosmain, Geneva: The Alpha-Cell in Type 1 and Type 2 Diabetes	
15:15 – 15:20	**Short Break**	(Foyer, Kursraum 1)

15:20 – 17:30	**Session 4:** **From Islets and Transplantation to the Artificial Pancreas**	(Auditorium Ettore Rossi)
	Chair: R. Lehmann, Zurich; C. Stettler, Bern	
15:20 – 16:00	R. Lehmann, Zurich: Long-Term Follow-Up of Simultaneous Islet-Kidney Transplantation	
16:00 – 16:25	N.S. Kenyon, Miami: Islet Transplantation from the Beginning to the Future	
16:25 – 17:05	C. Stettler, Bern: Artificial Pancreas - Role of Exercise and Food	
17:05 – 17:30	J. Bolinder, Stockholm: From Pancreas Transplantation to Diabetes Technologies	
17:30 – 17:50	**Coffee Break**	(Foyer, Kursraum 1)
17:50 – 18:50	**Satellite Symposium:** **Sugar and the Heart** *(sponsored by Astra Zeneca)*	(Auditorium Ettore Rossi)
	Speakers: M. Donath, Basel (Endocrinologist) and T. Burkhard, Basel (Cardiologist)	
20:00	**Dinner**	(Restaurant Gurten; Pavillon)

Friday, July 01, 2016 (Parallel Sessions)

10:45 – 12:05	**Parallel Session:** **Diabetes un Endocrine Disease** *supported by the Swiss Society of Endocrinology and Diabetes*	(Langhans Auditorium)
	Chair: E. Christ, Bern; F. Pralong, Lausanne	
10:45 – 11:05	C. Meier, Basel: Diabetes & Osteoporosis	
11:05 – 11:25	C. Henzen, Lucerne: Diabetes & Hyperparathyroidism	
11:25 – 11:45	S. Bilz, St. Gallen: Diabetes & Growth Hormone	
11:45 – 12:05	P. Wiesli, Frauenfeld: Diabetes & Cortisone	
13:30 – 15:40	**Parallel Session:** **Diabetes-Update für Berater/-innen** *(in German)*	(Langhans Auditorium)
13:30 – 14:00	E. Horat, Bern: Lösungsorientiert Kommunizieren	
14:00 – 14:30	R. Fricker, Bern: verschiedene Fazetten der Kohlenhydrate	
14:30 – 15: 00	L. Bally, Bern: Continuous Glucose Monitoring zur Therapieentscheidung	
15:00 – 15:30	B. Chappuis, Burgdorf: Neue Diabetesmedikamente - Wird nun Alles Besser?	

Saturday, July 02, 2016

08:15 – 09:30	**Session 5:** **Oral Presentations**	(Auditorium Ettore Rossi)
	Chair: E. Hatziagelaki, Athens; E. Standl, Munich	
08:15	Dehais et al.: GoCARB: A Computer Vision-Based Smartphone System for Carbohydrate Counting	
08:30	Dietrich et al.: Impaired Glucose Tolerance in Mice with β-Cell-Specific Deletion of PKBα	
08:45	Hohendorff et al.: Response to SGLT-2 Inhibitor May Be Altered in HNF1A-MODY.	
09:00	Holl et al.: Differential Use of Insulin Pumps in Patients with Type-1-Diabetes of Different Age-Groups: Analysis of the DPV (Diabetes Prospective Folllow-Up) Initiative	
09:15	Pesta et al.: Type II Musclefibers Have an Increased Potential for Reactive Oxygen Production	
09:30 – 10:30	**Session 6:** **From Obesity to Type-2 Diabetes**	(Auditorium Ettore Rossi)
	Chair: Z. Stanga, Bern; C. Herder, Dusseldorf	
09:30 – 09:50	A. Golay, Geneva: The Double Insulin Resistance	
09:50 – 10:10	M. Donath, Basel: Targeting Inflammation in Obesity to Prevent and Treat Type 2 Diabetes	
10:10 – 10:30	P. Gerber, Zurich: Fructose: Guilty or Innocent?	
10:30 – 11:00	**Coffee Break**	(Foyer, Kursraum 1)
11:00 – 12:20	**Session 7:** **Update on Pathophysiology of Diabetes**	(Auditorium Ettore Rossi)
	Chair: G. Spinas, Zurich; H. Schatz, Bochum	
11:00 – 11:20	N.C. Schloot, Dusseldorf: Autoimmunity in Human Type 1 Diabetes	
11:20 – 11:40	P. Maechler, Geneva: Mitochondrial Function and Insulin Secretion	
11:40 – 12:00	K. Ahmed, Zurich: MircoRNA and Islet Function	
12:00 – 12:20	J. Krützfeldt, Zurich: MicroRNA and Insulin Resistance	
12:20 – 12:40	**Closing Session** **Including Presentation of the Next Congress Venue**	(Auditorium Ettore Rossi)
12:40	**Farewell Apero**	(Foyer, Kursraum1)

Abstracts
Oral Presentation

Title:
GoCARB: A Computer Vision-Based Smartphone System for Carbohydrate Counting

Authors / Address of institution:
Joachim Dehais[1], Marios Anthimopoulos[1], Sergey Shevchik[1], Ransford Botwey[1], Daniel Rhyner[1,2], Lia Bally[2], Pieter Diem[2], Christoph Stettler[2], Stavroula Mougiakakou[1,2]
[1] ARTORG Center for Biomedical Engineering Research, University of Bern. Switzerland
[2] Department of Endocrinology, Diabetes and Clinical Nutrition, Bern University Hospital "Inselspital", Switzerland

Background / Introduction:
Estimating a meal's carbohydrate (CHO) counting is of importance in diabetes self-management. However, it remains a challenging task in daily life. GoCARB is a computer vision-based smartphone application designed to estimate meal's CHO content h with an error less than ±20 grams/meal and minimum user interaction.

Methods:
The GoCARB prototype was developed based on the assumptions that the plate is circular and shallow and the food items in the plate are not occluded. In a typical scenario, the user places a reference object (e.g. credit card) next to the plate and acquires two images using a smartphone's camera. Then, the different food items on the plate are segmented and recognized while their 3D shape is reconstructed. Based on the shape, the segmentation results and the reference object, the volume of each item is estimated. Finally, the CHO content is calculated by combining the food type with its volume, and using nutritional databases. GoCARB's validation involved a three-step procedure: i) testing in a laboratory setup with 24 dishes, ii) ple-clinical study involving 19 adults with T1D, and iii) randomized, prospective, single-center, two-period, with cross-over after one week clinical trial involving 20 adults with T1D under sensor-augmented pump therapy.

Results:
In the laboratory setup, GoCARB was able to estimate the CHO content of 24 meals with a mean absolute error of 6±8 CHO grams. In the preclinical study, each participant was asked to count the CHO content of each meal. Then, he/she was asked to estimate the CHO content by using GoCARB. A total of 114 estimates on 60 meals were used. The mean absolute error was 27.89 ± 38.20 CHO grams of CHO for individuals with T1D and 12.28 ± 9.56 CHO grams by using the GoCARB system. Participants also strongly supported using the software for daily counting. During the clinical trial, the participant's glucose levels, insulin intake, energy expenditure, and eating habits were gathered. These data were then processed to calculate useful diabetes management measures and the effect of GoCARB on them. An early analysis showed a positive influence for the use of GoCARB: the average and standard deviation of glucose level were lower, and so was the average increase in postprandial glucose.

Conclusion:
According to the three-step validation procedure the GoCARB system the CHO content errors below 20 grams and is significantly more accurate than the average individual with T1D. Furthermore, it seems that its usage positively impacts the glucose profile.

Title:
Impaired glucose tolerance in mice with ß-cell-specific deletion of PKBα

Authors / Address of institution:
M.G. Dietrich[1,2]; R.A. Zuellig[1]; F.C. Lucchini [3]; S. Wueest [3]; M. Niessen[1,2]; D. Konrad [3]; G.A. Spinas[1,2]; O. Tschopp[1,2]
[1] Division of Endocrinology, Diabetes & Clinical Nutrition, University Hospital Zurich, Switzerland
[2] Competence Center Personalized Medicine UZH/ETH, Zurich, Switzerland
[3] Division of Pediatric Endocrinology and Diabetology, University Children's Hospital Zurich, Switzerland

Background / Introduction:
Protein kinase B (PKB)/Akt is considered a key target downstream of insulin receptor substrate 2 (IRS2) in the regulation of pancreatic β-cell mass. There exist three isoforms of PKB, i.e. PKBα/Akt1, PKBβ/Akt2, and PKBγ/Akt3, which are all expressed in pancreatic β-cells. It is, however unclear, whether these isoforms exert differential effects with regard to functional β-cell mass. The aim of this study was to investigate in mice the effect of β-cell specific deletion of PKBα (βpkbαKO) on glucose homeostasis, β-cell function and β-cell mass.

Methods:
Mice were rendered insulin resistant by feeding a high-fat diet (HFD) and characterized metabolically by intraperitoneal glucose (ipGTT), insulin tolerance tests and hyperglycemic clamps. In addition, glucose-stimulated insulin secretion (GSIS) was assessed in isolated islets and islet morphology was studied in pancreatic tissue sections.

Results:
Western blot analysis showed that PKBα was normally expressed in control mice, but absent in β-cells from βpkbαKO mice. Under normal chow diet male βpkbαKO mice exhibited reduced glucose tolerance with significantly increased AUC (+22.6% ± 6.5%; $p \leq 0.05$) in adult live, i.e. at the age of 26 weeks. HFD accelerated the onset of impaired glucose tolerance with significantly increased AUC (+10.06% ± 3.6%; $p \leq 0.05$) already at age of 12 weeks (6 weeks on HFD). Plasma insulin levels during GTT and hyperglycemic clamps were reduced in HFD-fed βpkbαKO mice. However, GSIS was increased in islets from chow fed but decreased in islets from HFD-fed βpkbαKO mice. Preliminary analyses of pancreas morphology from 28 weeks old mice revealed a 50% decrease of β-cell area in βpkbαKO mice under chow and HFD as compared to control littermates.

Conclusion:
Thus, this study shows for the first time that β-cell specific loss of PKBα results in impaired glucose tolerance, potentially due to reduced β-cell mass. Whether the reduced β-cell mass in adulthood is the result of islet loss or of failure to form new islets, or even caused by impaired embryonic development is currently under investigation.

Title:
Response to SGLT-2 inhibitor may be altered in HNF1A-MODY.

Authors / Address of institution:
Hohendorff J, Szopa M, Skupien J, Klupa T, Malecki MT

Background / Introduction:
MODY accounts for 1-5 % of all diabetes cases and most of them are HNF1A- and GCK-MODY. Dietary intervention is generally sufficient to maintain good glycemic control in subjects with GCK gene mutation. HNF1A gene mutations affect insulin secretion to a greater extent. For patients with genetically confirmed HNF1A-MODY sulfonylurea therapy should be considered as the first-line treatment. It was shown that HNF1A controls SGLT2 (sodium-glucose co-transporter 2) expression which results in increased glycosuria in HNF1A-MODY patients. Therefore, response to SGLT2 inhibitors in HNF1A-MODY patients may be altered. In this pilot study, we aimed to assess differences in response to a single morning application of 10 mg dapagliflozin in HNF1A- and GCK-MODY patients.

Methods:
A total of 21 patients were included in the study: 11 with GCK-MODY and 10 with HNF1A-MODY. Dapagliflozin was added to patients current treatment regimens - all GCK-MODY subjects were on diet only, whereas HNF1A-MODY patients were on diet (1), SU (6), SU combined with metformin (2) and SU combined with 3U/d of insulin (1). Fasting plasma glucose (FPG), urine glucose concentration and urinary glucose-to-creatinine ratio (GCR) were measured in the morning of the administration day and the day after. Additionally, patients were asked to perform self-monitoring of blood glucose twice – on the administration day and the day before.

Results:
There were no differences in mean HbA1c (6,25; 6,06%) nor BMI (23,1; 24,6 kg/m^2) between the groups. GCK-MODY patients had higher mean FPG (6,81 vs. 5,66 mmol/l, p=0,0137). Mean reduction in FPG after dapagliflozin administration was 0,63 in GCK-MODY, whereas in HNF1A-MODY patients was 0,24 mmol/l (p=0,2367). This could suggest altered response to SGLT2 inhibitors in HNF1A-MODY due to impaired SGLT2 function. Moreover, we found a difference in median increment in GCR after SGLT2 inhibitor administration between GCK-MODY and HNF1A-MODY patients (24,5 vs.14,0 p=0,0447).

Conclusion:
To summarize, SGLT2 inhibitors seems to be less efficient in HNF1A-MODY than in GCK-MODY. This finding requires further studies.
Financial support: The study was supported by an EFSD New Horizons Programme award.

Title:
Differential use of Insulin Pumps in Patients with Type-1-diabetes of different Age-groups: Analysis of the DPV (Diabetes Prospective Follow-up) initiative with centers from Germany, Austria, Luxemburg and Switzerland

Authors / Address of institution:
Holl, Reinhard W; Bohn, Barbara (Ulm), Heidtmann Bettina (Hamburg), Hofer Sabine E (Innsbruck), Rosenbauer Joachim (Düsseldorf), Lilienthal Eggert (Bochum), Witsch Michael (Luxemburg), Zlamal-Fortunat, Sandra(Klagenfurt), Laimer, Markus (Bern)
Contact: Reinhard W. Holl, University of Ulm, Institute for Epidemiology and Medical Biometry, ZIBMT, Albert-Einstein-Allee 41, Germany

Background / Introduction:
Data on therapy options in real-life patient care are important to monitor trends in diabetes therapy as well as adherence to current guidelines together with short-term and long-term outcome. Increasing use of diabetes technology, including insulin pumps and continuous glucose monitoring, is one of the most dynamic trends in type-1 diabetes management during recent years. We investigated age-differences in the use of insulin pumps since the year 2000.

Methods:
The DPV registry is one of the largest ressources available on care and outcome of diabetes in Germany and Austria, including both pediatric and adult patients. Recently centers from Luxemburg (pediatrics) and Switzerland (internal medicine). In total, the registry includes 3.7 Million patient visits from 454,645 patients with diabetes. This abstract focusses on type-1-diabetes, with 2,167,530 visits from 108,052 patients. Use of insulin pumps was evaluated by year of treatment and age-group. A total of 445 specialized diabetes centers contributed data (258 pediatric, 187 internal medicine). SAS 9.4 was used for data analysis.

Results:
In total, 31,188 patients with type-1 diabetes using insulin pumps are included in the DPV registry. In adult patients (age > 18 years), pump use increase fom 24.1 % in the year 2000 to 36.2 % in 2015. In adolescents (12-18 years), was even more pronounced (2000: 5.8 %, 2015: 41.6 %). School-age patients (6-12 years) displayed an increase from 1.1 % of pump use in 2000 up to 53.9 % in 2015. The most striking pattern was observed in pre-school children (< 6 years of age): 0.8 % used insulin pumps in 2000, increasing up to 83.1 % in 2015.

Conclusion:
The use of CSII increased in all age-groups, however there was a clear age difference with later adoption of insulin pumps, but more rapid increase in this therapy for younger children. Today, the vast majority of toddlers uses insulin pumps. Population-based registries documenting the process and outcome of diabetes care, are a valuable tool to monitor longitudinal trends in real-life patient care.

Title:
Type II musclefibers have an increased potential for reactive oxygen species production

Authors / Address of institution:
Dominik Pesta, Tomas Jelenik, Michael Roden / Institute for Clinical Diabetology, Heinrich-Heine University Düsseldorf, German Diabetes Center, Düsseldorf, Germany

Background / Introduction:
Increased reactive oxygen species (ROS) production in skeletal muscle has been associated with the development of insulin resistance and type 2 diabetes (T2D). Preliminary evidence suggests that fast-twitch type II fibers may possess a higher potential for ROS production than slow-twitch type I fibers. First-degree relatives of patients with T2D have ~30% increased number of type II muscle fibers. Therefore, the connection between oxidative stress, impaired mitochondrial function, and insulin resistance warrants further investigation.

Methods:
Site-specific ROS production of three main sites (CIQ, CIIF, CIIIQo) was assessed by superoxide Amplex Red fluorescence assay in two muscles with a different fiber spectrum from slow to fast (soleus, white gastrocnemius) in wildtype mice (C57BL/6J). Mitochondrial content was determined by citrate synthase activity (CSA).

Results:
We find that ROS production per wet weight is higher in soleus than in white gastrocnemius at CIQ with a trend at CIIF and no difference at CIIIQo. When ROS production is normalized for mitochondrial content, ROS production at CIQ is 50% higher in white gastrocnemius than in soleus with a similar strong trend at CIIIQo and no difference at CIIF.

Conclusion:
Our results suggest intrinsic differences in the potential for ROS production between fast- and slow-twitch muscle fibers which are independent of mitochondrial content.

Abstracts
Poster Presentation

Title:

Clinical Outcomes in Asian and non-Asian People with Type 2 Diabetes Initiating Glargine 100 Units/mL (Gla-100) Therapy: Results of a Pooled Analysis from 16 RCTs

Authors / Address of institution:

Juliana CN Chan[1], Pongamorn Bunnag[2], Siew Pheng Chan[3], Iris Thiele Isip Tan[4], Shih-Tzer Tsai[5], Ling Gao[6], Wolfgang Landgraf[7].
[1]The Chinese University of Hong Kong, Hong Kong Special Administrative Region, People's Republic of China; [2]Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; [3]University of Malaya Medical Centre, Kuala Lumpur, Malaysia; [4]University of the Philippines, Manila, Philippines; [5]Cheng Hsin General Hospital, Taipei, Taiwan; [6]Analysta Inc., Somerset, NJ, USA; [7]Sanofi, Frankfurt, Germany. E-mail address for correspondence: Wolfgang.Landgraf@sanofi.com.

Background / Introduction:

Type 2 diabetes (T2DM) is an epidemic disease in Asia, with a younger age and lower BMI at diagnosis in Asians vs non-Asians.

Methods:

This patient-level analysis compared outcomes in Asians and non-Asians with T2DM from 16 RCTs (target FPG ≤ 100 mg/dL, ≥ 24-week duration) adding Gla-100 to OADs. Data from Asians and non-Asians were compared overall and by concomitant metformin (MET) plus sulphonylurea (SU) therapy at baseline and Week 24.

Results:

Of 3,586 study participants, 235 were Asian. Among OADs, MET+SU was the most common co-treatment with Gla-100. Outcomes at Week 24 for overall and MET+SU subgroups are shown in the Table. Asians were younger, had a lower BMI and FPG, but similar baseline HbA1c vs non-Asians. Asians had a statistically significant higher adjusted mean HbA1c at week 24 and were less likely to achieve target HbA1c <7.0%, but more Asians had FPG ≤100 mg/dL compared with non-Asians. Final Gla-100 doses and hypoglycemia event rates were similar in Asians and non-Asians. Lower weight gain was observed in Asians (P = 0.01). The results of the MET+SU subgroup reflected those of the overall population.

Conclusion:

This post-hoc analysis suggests that at similar Gla-100 doses and hypoglycemia frequency, HbA1c control in Asian T2DM patients appears poorer compared with non-Asian patients, despite better FPG control. More studies are needed to explore potential differences in treatment responses between Asian and non-Asian T2DM patients.

Table. Clinical Outcomes in Asian and non-Asian People With T2D Initiating Gla-100 Therapy

	Gla-100 Overall			Gla-100 + MET + SU		
Parameter (SD)	**Asian (n = 235)**	**Non-Asian (n = 3,351)**	***P* Value**	**Asian (n = 111)**	**Non-Asian (n = 1,513)**	***P* Value**
Baseline						
Age, years	53.7 (9.0)	57.9 (9.7)	< 0.001	54.1 (8.8)	58.5 (9.1)	< 0.001
Diabetes duration, years	8.9 (6.0)	8.9 (6.2)	0.92	9.6 (4.8)	9.4 (6.3)	0.74
Weight, kg	70.4 (12.6)	87.3 (18.1)	< 0.001	70.1 (13.2)	88.6 (17.0)	< 0.001
BMI, kg/m^2	27.1 (3.9)	30.8 (5.3)	< 0.001	27.3 (4.3)	31.2 (4.9)	< 0.001
HbA1c, %	8.6 (1.0)	8.7 (1.1)	0.08	8.4 (0.9)	8.6 (1.0)	0.04
FPG, mg/dL	169 (46)	194 (55)	< 0.001	160 (38)	189 (52)	< 0.001
Insulin dose, U/kg	0.18 (0.04)	0.16 (0.08)	< 0.001	0.17 (0.04)	0.14 (0.05)	< 0.001
Week 24 endpoints:						
Adjusted HbA1c, %	7.42 (0.06)	7.16 (0.02)	< 0.001	7.16 (0.08)	7.07 (0.02)	0.27
Adjusted HbA1c change from baseline	−1.30 (0.06)	−1.55 (0.02)	< 0.001	−1.41 (0.08)	−1.50 (0.02)	0.27
HbA1c ≤ 7.0 %, n (%)	90 (41.9)	1605 (50.7)	< 0.001	44 (43.1)	783 (53.8)	0.14
Adjusted FPG change from baseline, mg/dL	−78.1 (2.6)	−75.2 (0.7)	0.27	−74.4 (3.7)	−68.3 (0.9)	0.11
FPG ≤ 100 mg/dL, n (%)	101 (47.6)	1076 (34.0)	0.21	44 (44.9)	468 (32.5)	0.37
Adjusted hypoglycemia[a], events per patient-year	4.3 (0.6)	5.5 (0.2)	0.09	6.5 (1.1)	7.4 (0.3)	0.45
Adjusted weight change from baseline, kg	1.3 (0.2)	1.9 (0.1)	0.01	1.4 (0.3)	1.8 (0.1)	0.25
Adjusted insulin dose, U/kg	0.47 (0.02)	0.45 (0.00)	0.16	0.36 (0.02)	0.41 (0.01)	0.045

Data presented represent mean (SD) for baseline and adjusted mean (SE) for Week 24 endpoint, except for items n (%).
[a]Overall hypoglycemia defined as PG <70 mg/dL or third-party assistance required.

Study supported by Sanofi

Data will be presented at ADA 2016, Saturday June 10-14, 2016, New Orleans, Louisiana

Title:

Patient Characteristics and Clinical Outcomes Associated With Hypoglycemia Frequency During Titration of Insulin Glargine 100 units/mL (Gla-100) in People With Type 2 Diabetes (T2D)

Authors / Address of institution:

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Background / Introduction: Hypoglycemia during insulin initiation and intensification can be a barrier to dose optimization and achievement of glycemic control targets.

Methods: This post-hoc subject-level analysis examined standardized data from 16 RCTs (FPG target ≤ 100 mg/dL, ≥ 24 weeks duration) adding Gla-100 to OADs in insulin-naive people with T2D. The impact was studied of overall hypoglycemia frequency (confirmed PG < 70 mg/dL or assistance required, stratified according to 0, 1−3, 4−6, or > 6 events during titration from Weeks 0−8) on glycemic outcomes and insulin dose at Week 24.

Results: Data from 3,549 participants were analyzed. Group size declined as hypoglycemia frequency increased but mean age was similar (58 years) across all groups. Those with > 4 hypoglycemic events during titration had the lowest baseline body weight, FPG, and HbA1c, and longer diabetes duration (Table). In contrast, those experiencing less hypoglycemia (≤ 3 events) had higher BMI, FPG and HbA1c at onset with a greater change in insulin dose from baseline to Week 24.

Conclusion: Lower hypoglycemia incidence occurs during insulin titration in people with T2D with a greater insulin resistance (higher insulin dose requirement and smaller HbA1c reduction), in contrast to people experiencing more hypoglycemia during titration with greater HbA1c reduction.

Table. Patient Characteristics Stratified by Frequency of Hypoglycemic Events During Gla-100 Titration

	Frequency of Hypoglycemic Events During Titration (Week 0–8)			
Parameter	**0 n = 2,573**	**1–3 n = 732**	**4–6 n = 152**	**> 6 n = 92**
Duration of diabetes, years	8.6 (6.0)	9.5 (6.4)	10.2 (6.5)	9.9 (7.4)
Baseline body weight, kg	87.7 (18.5)	83.3 (17.4)	77.4 (14.6)	77.8 (15.1)
Baseline BMI, kg/m^2	31.0 (5.3)	29.6 (4.9)	28.3 (4.5)	28.4 (4.5)
Baseline FPG, mg/dL	194 (54)	187 (52)	186 (64)	184 (55)
Baseline HbA1c, %	8.8 (1.1)	8.6 (1.0)	8.5 (1.0)	8.5 (0.9)
Baseline insulin dose, U/kg	0.2 (0.1)	0.2 (0.1)	0.2 (0.1)	0.2 (0.1)
Week 24 HbA1c, %*	7.2 (1.04)	7.0 (0.95)	7.1 (0.87)	7.0 (0.91)
HbA1c change from BL to week 24, %*	−1.5 (1.2)	−1.5 (1.1)	−1.4 (1.0)	−1.5 (1.0)
Insulin dose change from BL to week 24, U/kg†	0.31 (0.26)	0.20 (0.19)	0.12 (0.16)	0.07 (0.14)

*0: n = 2,486; 1–3: n = 718; 4–6: n = 152; > 6: n = 91.
†0: n = 2,573; 1–3: n = 732; 4–6: n = 152; >6: n = 92.
Data presented represent mean (SD). SD, standard deviation; BL, baseline

Study supported by Sanofi

Data will be presented at ADA 2016, Saturday June 10-14, 2016, New Orleans, Louisiana

Title:

Effect of glucose lowering treatment on lipid profile in people with type 2 diabetes (T2DM): relationship to lipid lowering therapy

Authors / Address of institution:

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Background / Introduction: Dyslipidemia is a major risk factor for cardiovascular disease (CVD), being the major cause of mortality in T2DM.

Methods: This post-hoc patient-level analysis included data from 11 RCTs (target FPG ≤100 mg/dL, ≥24 week duration) conducted with insulin glargine 100 units/ml (Gla-100) vs comparator antihyperglycemic drugs from 1999 to 2008. The effects of pooled glucose lowering therapy (GLT) on lipid status at baseline and 24 weeks were examined in patients with diagnosed CVD at BL and receiving lipid lowering therapy (LLT) at discretion of physicians, patients with CVD not receiving LLT and control people without CVD, not receiving LLT.

Results: Only 41% (n=1,940) of all T2DM study participants ± CVD (n=4,768) were treated with LLT despite being considered at high CV risk and 2,828 did not receive LLT. LLT included statins (88%), fibrates (11%), and others (10%). 97% (with LLT) and 63% (without LLT) had CVD at study entry with LDL-C, non HDL-C, triglycerides (TG) levels above lipid targets recommendations at baseline and week 24, whatever LLT (Table). After 24 weeks of GLT, non–HDL-C and TG slightly improved; LDL-C, HDL-C levels remained almost unchanged, irrespective of LLT use. Importantly, only 51% of those with T2DM and CVD received LLT as recommended (AHA/ADA 2015).

Conclusion: Our data suggest modest improvement on non-HDL-C, TG levels with GLT in T2DM study participants with CVD and the need to treat people with T2DM optimally with LLT according to current recommendations.

	Lipid-lowering therapy during trial		No lipid-lowering therapy during trial			
	Diagnosed with CVD at baseline (n = 1,885)		Diagnosed with CVD at baseline (n = 1,787)		Without CVD diagnosis at baseline (n =1,041)	
Glucose lowering treatment	Gla-100: 51% other insulins: 16% NPH: 14% OADs: 19%		Gla-100: 53% other insulins: 10% NPH: 17% OADs: 20%		Gla-100: 54% other insulins: 7% NPH: 24% OADs: 15%	
	Baseline	Change from baseline to week 24	Baseline	Change from baseline to week 24	Baseline	Change from baseline to week 24
HbA1c, %	8.7 (1.02)	-1.4 (1.13)	8.8 (1.05)	-1.5 (1.19)	9.0 (1.09)	-1.6 (1.24)
Non-HDL-C, mg/dL	142.85 (48.42)	-9.10 (39.67)	159.78 (41.92)	-5.20 (29.57)	151.04 (50.31)	-3.85 (43.34)
LDL-C, mg/dL	99.94 (37.05)	-0.98 (30.48)	120.83 (36.39)	1.51 (27.42)	116.31 (32.96)	0.51 (25.96)
HDL-C, mg/dL	43.83 (11.42)	0.32 (7.17)	45.69 (13.30)	0.56 (10.12)	45.27 (13.08)	0.36 (10.58)
Triglycerides, mg/dL	241.40 (247.69)	-51.20 (220.81)	210.99 (163.16)	-38.84 (141.93)	181.51 (129.15)	-25.83 (106.05)
C-Peptide (nmol/L)	1.19 (0.60)		1.15 (0.59)		1.00 (0.60)	

Data represent mean (SD); HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol. $P < 0.05$ between patients treated with lipid lowering therapy vs not treated for HbA1c and all lipid parameters at baseline and change to week 24, except for triglycerides which was significant ($P < 0.05$) at baseline only.

Study supported by Sanofi

Data will be presented at ADA 2016, Saturday June 10-14, 2016, New Orleans, Louisiana

Title:
Biomarkers of subclinical inflammation are associated with cardiac autonomic dysfunction in recent-onset type 2 but not type 1 diabetes

Authors / Address of institution:
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[#] M.R. and D.Z. contributed equally to this work.

Background / Introduction:
Cardiovascular autonomic neuropathy is a common but underestimated diabetes-related disorder. Associations between cardiovascular autonomic dysfunction and subclinical inflammation, both risk factors of diabetic comorbidities and mortality, have been proposed in non-diabetic populations, while data for type 1 and type 2 diabetes are conflicting. Our aim was to investigate associations between inflammation-related biomarkers and cardiac autonomic dysfunction in rencently diagnosed diabetes patients.

Methods:
We characterised the associations between seven biomarkers of subclinical inflammation and cardiac autonomic dysfunction based on heart rate variability (HRV) and cardiovascular autonomic reflex tests (CARTs) in 161 individuals with type 1 and 352 individuals with type 2 diabetes (time since diagnosis of diabetes <1 year). Analyses were adjusted for age, sex, anthropometric, metabolic and lifestyle factors, medication and cardiovascular comorbidities.

Results:
In individuals with type 2 diabetes, higher serum interleukin (IL)-18 was associated with lower vagal activity (P≤0.015 for association with CARTs), whereas higher levels of total and high-molecular-weight adiponectin showed associations with very-low-frequency power, an indicator of reduced sympathetic activity (P≤0.014). Higher levels of soluble intercellular adhesion molecule-1 were associated with indicators of both lower vagal (P=0.025) and sympathetic (P=0.008) tone, soluble E-selectin with one indicator of lower vagal activity (P=0.047). Serum C-reactive protein and IL-6 were also related to cardiac autonomic dysfunction, but these associations were explained by confounding factors. No consistent associations were found in individuals with type 1 diabetes.

Conclusion:
Biomarkers of inflammation were differentially associated with diminished cardiac autonomic dysfunction as early as in recent-onset type 2 but not type 1 diabetes.

Title:
Online adaptive models for personalized prediction of glucose profile in individuals with type 1 diabetes

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Background / Introduction:
The use of personalized, data-driven models for the real-time prediction of glucose profile in individuals with type 1 diabetes (T1D) under sensor-augmented pump (SAP) therapy is of imminence importance for diabetes self-management. Scope of the present research is to investigate how to tackle issues related to the accuracy of the glucose predictions and time-lags (TL) between predicted and measured signals especially in higher prediction horizons (PHs).

Methods:
Sensor glucose (G), insulin pump (I), food intake (CHO), and physical activity (PA) data from six individuals with T1D under SAP were used (age: 22-29 years; HbA1c: 6.83 ± 0.75%; body mass index: 24.79 ± 4.71 kg/m2). The data provided input to a computational framework composed by two layers: Prediction and correction. The prediction layer involves two data-driven models (corrected ARX model - cARX; Recurrent Neural Network trained by Unscented Kalman filter - uRNN). All models are online adaptive and can be personalized to each individual with T1D. The outputs of all models are corrected by an extreme learning machine (ELM) constituting the correction layer. The different models were evaluated on the basis of root mean square error (RMSE) and TL between predicted and real signals for PH=15, 30 and 45 minutes.

Results:
The results indicate that the use of lifestyle information (CHO and PA) along with data from the SAP therapy improves the glucose predictions especially in terms of TL and in the case of increased PH. Furthermore, ELM independently of the used model, positively impacts the prediction accuracy and reduces the TL for all the PHs. Finally, the cARX model fed with lifestyle and SAP data, along with an ELM, achieved lower TL over all the examined models and for all PHs with mean RMSE values of 9.4 (1.52) mg/dL and mean TL of 4.2 (2.04) min for PH=15 min, 19.2 (5.02) mg/dL and 10 (3.16) min for PH=30 min and 23.4 (5.20) mg/dL and 9.2 (5.85) min for PH=45 min.

Conclusion:
The finding of the presented work need to be confirmed in a larger dataset. The best performing setup will be integrated to a system for alarm generation whenever a hypoglycemic event is predicted.

Title: Impact of OADs on Hypoglycemia Frequency During Titration With Insulin Glargine 100 units/mL (Gla-100) in Type 2 Diabetes (T2D)

Authors / Address of institution:

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Background / Introduction: Hypoglycemia during insulin initiation and intensification can be a barrier to dose optimization and achievement of glycemic control targets.

Methods: This post-hoc subject-level analysis examined standardized data from 16 RCTs (FPG target ≤ 100 mg/dL, ≥ 24 weeks duration) adding Gla-100 to OADs in people with T2D. The impact of metformin (MET), sulfonylurea (SU), or MET + SU on overall hypoglycemia frequency (confirmed PG < 70 mg/dL or assistance required) stratified according to 0, 1–3, 4–6, or > 6 events during insulin dose titration from Weeks 0–8 was assessed; efficacy and insulin dose change at Week 24 were also examined.

Results: Data from 3,153 people receiving either MET (n = 623), SU (n = 906), or MET + SU (n = 1,624) in combination with Gla-100 for 24 weeks were analyzed. The concomitant OAD to which Gla-100 is added has a differential effect on HbA1c reduction. MET-treated subjects had the shortest diabetes duration and highest baseline BMI; the longest diabetes duration and lowest BMI were seen in the SU-only treated group (Table). In all OAD subgroups the majority experienced ≤ 3 hypoglycemic events during titration. The frequency of hypoglycemia was inversely related to the baseline BMI in all but the MET + SU-treated group with > 6 events. The adjusted insulin dose change from baseline was lowest in those with more hypoglycemic events, irrespective of OAD treatment.

Conclusion: In people with T2D, OADs co-administered with basal insulin therapy influence efficacy outcomes and overall hypoglycemia risk during the early period of insulin dose titration.

Table: Patient Characteristics Stratified by Frequency of Hypoglycemic Events and Concomitant OAD During Gla-100 Titration

Parameter	Glargine + OAD subgroup	Frequency of Hypoglycemic Events (PG < 70 mg/dL) During Titration (Week 0–8)			
		0	1–3	4–6	> 6
Number of people, N (%)	MET MET + SU SU	535 (85.9) 1047 (64.5) 683 (75.4)	75 (12.0) 421 (25.9) 168 (18.5)	6 (1.0) 100 (6.2) 35 (3.9)	7 (1.1) 56 (3.4) 20 (2.2)
Duration of diabetes, years	MET MET + SU SU	6.9 (5.3) 9.2 (6.0) 9.5 (6.6)	9.1 (6.9) 9.8 (6.3) 9.6 (6.8)	11.4 (8.8) 10.0 (6.4) 10.2 (6.6)	11.5 (6.9) 10.6 (8.4) 8.0 (5.2)
Baseline BMI, kg/m^2	MET MET + SU SU	31.8 (5.7) 31.4 (5.0) 29.6 (5.2)	29.3 (4.9) 30.4 (4.8) 27.7 (4.6)	27.6 (5.0) 28.7 (4.4) 27.0 (3.9)	26.0 (4.4) 29.7 (4.5) 25.9 (4.1)
Baseline FPG, mg/dL	MET MET + SU SU	187 (54) 192 (52) 202 (57)	177 (53) 180 (48) 206 (58)	152 (28) 176 (63) 222 (66)	178 (49) 163 (41) 242 (59)
Baseline HbA1c, %	MET MET + SU SU	8.7 (1.1) 8.7 (1.0) 9.0 (1.1)	8.4 (1.0) 8.4 (0.9) 8.9 (1.0)	8.5 (0.8) 8.4 (0.9) 9.1 (1.1)	9.0 (1.0) 8.2 (0.8) 9.3 (0.7)
HbA1c change from baseline to Week 24, %	MET MET + SU SU	−1.7 (1.2) −1.5 (1.1) −1.4 (1.2)	−1.6 (1.3) −1.5 (1.0) −1.5 (1.3)	−1.1 (1.0) −1.4 (1.0) −1.6 (1.2)	−1.4 (1.5) −1.4 (0.8) −2.1 (1.1)
Insulin dose change from baseline to Week 24, U/kg	MET MET + SU SU	0.37 (0.28) 0.31 (0.26) 0.26 (0.22)	0.20 (0.19) 0.20 (0.19) 0.16 (0.19)	0.08 (0.06) 0.16 (0.15) 0.02 (0.15)	0.07 (0.09) 0.08 (0.13) -0.01 (0.17)

Data presented represent mean (SD) unless otherwise specified. SD, standard deviation. SE, standard error.

Data will be presented at ADA 2016, Saturday June 10-14, 2016, New Orleans, Louisiana

Title:
Comparable effects of high-intensity interval training and detraining on physical capacity and pulmonary function in obese glucose-tolerant persons and patients with type 2 diabetes

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Background / Introduction:
Observational studies have shown that type 2 diabetes (T2D) is associated with reduced pulmonary function. Moreover, interventional studies have shown that exercise can improve lung function in patients with T2D. The present study tests the hypothesis that low-volume high-intensity interval training (HIIT), as an effective and time-efficient alternative to conventional exercise programs, improves physical capacity and pulmonary performance in T2D.

Methods:
Twelve sedentary male volunteers with T2D (age: 57±5 years, body mass index (BMI): 31.6±2.2 kg*m-2, known diabetes duration: 6±2 years, HbA1c: 55.0±10.5 mmol*mol-1) and 5 sedentary male glucose-tolerant controls (CON) (age: 55±2 years, BMI: 30.7±2.3 kg*m-2, HbA1c: 36.0±2.4 mmol*mol-1) underwent a 12-week HIIT using bicycle ergometers with a subsequent 4-weeks detraining period. Both groups did not differ in age, sex and BMI. Physical capacity was assessed from oxygen consumption at maximum (VO2max), peak oxygen pulse (CO) and maximum performance (Wattmax). Lung function was assessed by determining forced vital capacity (FVC), forced expiratory volume in one second (FEV1), maximum ventilation (VE) and breathing frequency (BF).

Results:
Compared to CON, patients with T2D showed no difference in parameters of physical capacity (e.g. VO2max or Wattmax) and lung function (e.g. FEV1 or FVC) at baseline, except for a reduced VE ($P<0.05$). After 12 weeks of HIIT, patients with T2D increased their lung function (FVC (+0.47±0.36 l), FEV1 (+0.27±0.19 l), VE (+19±17 l*min-1) and BF (+8±6 min-1; all $P<0.01$)) and physical capacity (VO2max (+4.4±1.8 ml*min-1*kg-1), Wattmax (+35±11 W) and CO (+2.5±2.5 ml*beat-1), all $P<0.01$), but showed no altered training response compared to CON. Four weeks of training pause showed no difference of detraining effect in parameters of physical capacity and lung function between CON and patients with T2D.

Conclusion:
In conclusion, 12-weeks HIIT improves physical and pulmonary performance in T2D and these changes show no difference compared to CON, even after 4 weeks of detraining.

Title:
Adiponectin and insulin sensitivity of adipose tissue in patients with cystic fibrosis

Authors / Address of institution:
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Background / Introduction:
Wasting is associated with increased adiponectin (ADN), an anti-inflammatory, insulin-sensitizing adipokine. Cystic fibrosis (CF) is a multi-organ disease characterized by inflammation, wasting and impaired insulin production. We assessed ADN and its high molecular weight (HMW) multimer form, and we measured venous plasma glucose (PG), serum insulin and free fatty acids (FFA) during an oral glucose tolerance test (oGTT) in patients with CF suffering from end stage lung disease.

Methods:
Over 10 years, consecutive CF patients were included and had evaluation with regard to lung transplantation. Patients (unless known for previous fasting PG (FPG) ≥7mM or insulin treatment, or on corticosteroids) and a control group of healthy subjects underwent an oGTT, and the insulinogenic index (IGI) was calculated as proposed by Wareham. Whole body and especially adipose tissue insulin sensitivity was estimated by calculating insulin resistance/sensitivity indices as proposed by Matthews (HOMA1-IR), Matsuda and DeFronzo (ISIcomp) and by Belfiore (ISIfat). ADN and its HMW form were measured by EIA, insulin by RIA, and FFA by a colorimetric assay. Data are expressed as mean±SD.

Results:
oGTT was performed in 47 CF patients (22 male; age 26±9y) and 34 controls (19 male; age 31±10y). CF patients had lower BMI (18.6±3.5kg/m2) than the controls (23.5±4.4kg/m2). FPG, HOMA1-IR and ISIcomp were similar in patients and in controls. IGI was lower and the 2hPG was higher in CF patients than in controls (18.6±12.3 vs 62.2±39.2pM/mM; 10.1±4.5 vs 6.0±1.3mM). During oGTT, FFA decreased from 0.59±0.32 (fasting) to 0.13±0.09mM (after 2h) in CF patients and from 0.60±0.44 to 0.12±0.10mM in controls. ISIfat was 1.04±0.27 in CF patients and 1.00±0.34 in controls. Total (and especially HMW-) ADN was higher in CF patients than in controls (10.4±3.8 vs 7.9±3.5mg/l; HMW% of total, 51±10 vs 38±11). There was a positive correlation of total adiponectin and its HMW form ($p<0.0001$).

Conclusion:
ADN (particularly HMW-ADN) levels are higher in CF patients than in controls. Despite markedly impaired insulin secretion, FFA were suppressed to a similar extent in CF patients as in the controls. Residual insulin (in the face of apparently normal insulin sensitivity and in the context of increased energy expenditure) appears to be sufficient for maintaining FFA homeostasis in patients with CF.

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